# Identification of Emerging Subpopulations Susceptible to Adverse Health Effects Associated with Particulate Air Pollution Exposure

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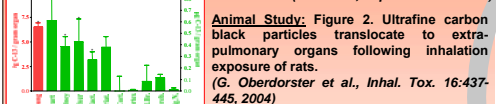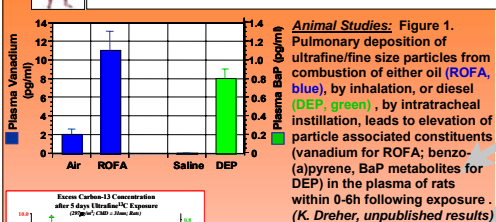A. Zanobetti, M. O'Neil, J. Schwartz, Harvard School of Public Health, Boston, MA
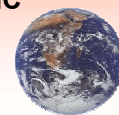
SCIENTIFIC QUESTIONS

Epidemiology, clinical, and toxicological studies have demonstrated the ability of ambient air particulate matter (PM) exposure to induce pulmonary as well as a variety of extra-pulmonary health effects ranging from alterations in hematological parameters to cardiac function. These findings raise the following questions:
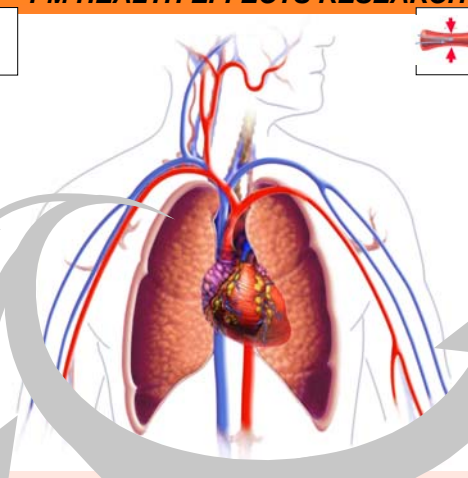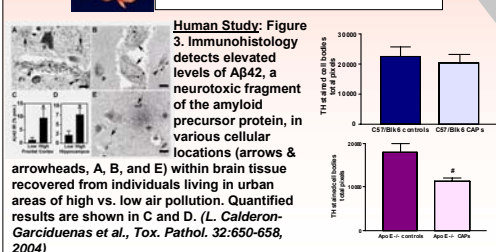
1) what are the PM properties and mechanism(s) of injury responsible for adverse extra-pulmonary PM health effects within existing and newly identified susceptible subpopulations?

2) do additional susceptible subpopulations exist due to the ability of pulmonary deposited PM to induce adverse extra-pulmonary health effects?

3) what are the sensitivity factors, or effect modifiers, within newly identified PM susceptible subpopulations?
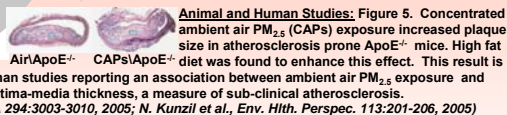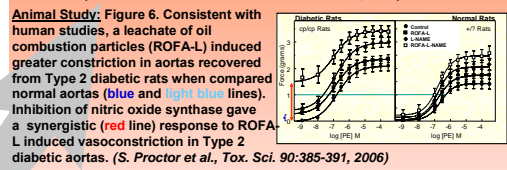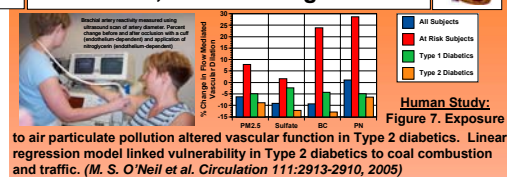
PM HEALTH EFFECTS RESEARCH

Exposure: Systemic Delivery of PM & Bioavailable Constituents

Animal Studies: Figure 1. Pulmonary deposition of ultrafine/fine size particles from combustion of either oil (ROFA, blue), by inhalation, or diesel (DEP, green), by intratracheal instillation, leads to elevation of particle associated constituents (vanadium for ROFA; benzo-(a)pyrene, BaP metabolites for DEP) in the plasma of rats within 0-6h following exposure . (K. Dreher, unpublished results)

Animal Study: Figure 2. Ultrafine carbon black particles translocate to extra-pulmonary organs following inhalation exposure of rats. (G. Oberdorster et al., Inhal. Tox. 16:437-445, 2004)

Neurological Effects: Brain Lesions

Human Study: Figure 3. Immunohistology detects elevated levels of $A\beta42$, a neurotoxic fragment of the amyloid precursor protein, in various cellular locations (arrows & arrowheads, A, B, and E) within brain tissue recovered from individuals living in urban areas of high vs. low air pollution. Quantified results are shown in C and D. (L. Calderon-Garciduenas et al., Tox. Pathol. 32:650-658, 2004)

Animal Study: Figure 4. Consistent with human studies, exposure to concentrated ambient air $PM_{2.5}$ decreases dopaminergic neurons in brain tissue of cardiovascular compromised (ApoE $^{-/-}$) but not healthy (C57BL6) mice. (B. Veronesi et al., Inhal. Tox.17:235-241, 2005)

Cardiovascular Effects: Vascular Function, Disease Progression

Human Study: Figure 7. Exposure to air particulate pollution altered vascular function in Type 2 diabetics. Linear regression model linked vulnerability in Type 2 diabetics to coal combustion and traffic. (M. S. O'Neil et al. Circulation 111:2913-2910, 2005)

Animal Study: Figure 6. Consistent with human studies, a leachate of oil combustion particles (ROFA-L) induced greater constriction in aortas recovered from Type 2 diabetic rats when compared normal aortas (blue and light blue lines). Inhibition of nitric oxide synthase gave a synergistic (red line) response to ROFA-L induced vasoconstriction in Type 2 diabetic aortas. (S. Proctor et al., Tox. Sci. 90:385-391, 2006)

Air\ApoE$^{-/-}$ CAPs\ApoE$^{-/-}$

Animal and Human Studies: Figure 5. Concentrated ambient air $PM_{2.5}$ (CAPs) exposure increased plaque size in atherosclerosis prone ApoE $^{-/-}$ mice. High fat diet was found to enhance this effect. This result is consistent with human studies reporting an association between ambient air $PM_{2.5}$ exposure and increased carotid intima-media thickness, a measure of sub-clinical atherosclerosis. (Q. Sun et al., JAMA 294:3003-3010, 2005; N. Kunzil et al., Env. Hlth. Perspec. 113:201-206, 2005)

Reproductive Effects: Birth Defects and Preterm Births

● Epidemiology Study: A seven county study of air quality and births in Texas from 1997-2000 reported an association between PM_{10} and atrial septal defects was observed when comparing high vs. low quartiles of exposure (OR=2.27; 95% CI:1.43, 3.60). (S. M. Gilboa et al., Am. J. Epidemiol. 162:238-252, 2005)

● Epidemiology Study: A time series analysis of air pollution and preterm births in Pennsylvania, from 1997-2001, reported an increased risk for preterm delivery with exposure to: 1) PM_{10} in the 6 weeks before birth, RR=1.07, 95% CI: 0.98-1.18 per 50 μg/m³ and PM_{10} 2 and 5 days before birth, RR=1.10, 95% CI:1.00-1.21 and RR=1.07, 95% CI:0.98-1.18. (S. K. Sagiv et al., Env. Hlth. Perspec.113:602-606, 2005)

PM HEALTH EFFECTS: RESULTS, FUTURE RESEARCH AND IMPACT

Table 1: Economic Impact of Disease		
DISEASE (Related Syndrome)	POPULATION EFFECTED (# in million)	COSTS ($ in billion)
Heart Disease (Metabolic Syndrome)	70.1 (47)	$393.5
Type 2 Diabetes[2] (Impaired Glucose Metabolism)	18 (20)	$132.8
Obesity[2]	135	$133
Alzheimer	4.5	$100.7
Premature Births	0.48	$1.2
Birth Defects[3,4]	0.15	$8
Total	228.23 (67)	$769.2

1. 2005 costs include: care; prevention; research; absenteeism & lost productivity .
2. Diabetes and Obesity (70% of whom become diabetic) are reaching epidemic levels.
3. National Research Council estimates 3% are related to environmental factors.
4. Birth defects have risen 27% since 1981.

● PM exposure leads to systemic delivery of particles and associated bioavailable constituents producing systemic health effects which may impact a variety of newly susceptible subpopulations.

● Integrated epidemiological, clinical, and toxicological research efforts are needed to:

1) ensure susceptible subpopulations are identified and characterized;

2) identify PM properties responsible for adverse health effects within newly identified susceptible subpopulations in order to link health effects to sources;

3) determine mechanism(s) of injury and dose-response relationships associated with the adverse PM health effects in newly identified susceptible subpopulations.

● Research will provide critical information to the Agency in order to:

1) set PM standards based on sound science that protect the most sensitive populations, as mandated by the Clean Air Act, and inform the Air Quality Index;

2) implement control strategies for causal PM sources which may provide significant savings in health care costs associated with diseases listed in Table 1 by determining the impact of PM on the progression and\or exacerbation of these diseases and setting standards that provide adequate protection.

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